DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

Via Federal Express

WARNING LETTER

APR 27 2001

Donald R. Johnson, M.D.
Carolina Spine Institute
900 Bowman Road, Suite 300
Mt. Pleasant, South Carolina 29464

Dear Dr. Johnson:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site and requests from you a prompt reply informing us of your corrective actions. You participated as a clinical investigator in a study entitled, [redacted] (Protocol [redacted]), sponsored by [redacted] to investigate the device [redacted]. Data from the study conducted at your site was submitted to the FDA in support of the premarket approval application, PMA [redacted]

During the period of February 14 through February 22, 2000, you were visited by Janice L. King, an investigator from the FDA's Atlanta District Office. The purpose of Ms. King's visit was to conduct an inspection to determine whether your activities and procedures as a clinical investigator for the [redacted] study, complied with applicable regulations. This product is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

This inspection was conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approval (PMA), and Premarket Notification (510(k)) submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

We have completed our review of the inspection report submitted by the Atlanta District Office. The report reveals significant violations of the requirements under Title 21, Code of Federal Regulations (21 CFR), Part 50 - Protection of Human Subjects, and 21 CFR Part 812 - Investigational Device Exemptions. These violations are listed on the Form FDA 483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. The violations noted on the Form FDA 483 and our subsequent review of the inspection report are summarized below:

1. **Failure to prepare and submit complete, accurate, and timely reports of unanticipated adverse device effects *(21 CFR 812.110(b) and 21 CFR 812.150(a)(1)).***

   You failed to submit to the institutional review boards (IRBs) complete, accurate, and timely reports of unanticipated adverse device effects experienced by patients enrolled in the [redacted] study. For example, patient [redacted] experienced a dural tear, cerebrospinal fluid (CSF) leak at the surgical site, and severe headache necessitating surgical repair. This event was reported on the case report form SAE dated [redacted] as a severe event requiring hospitalization and intervention to prevent permanent impairment or damage. However, this unanticipated adverse device effect was not reported to the IRB as soon as possible but in no event later than ten (10) working days after you first learned of the effect.

2. **Failure to conduct an investigation in accordance with the investigational plan *(21 CFR 812.100, 21 CFR 812.110(b), and 21 CFR 812.140(a)(4)).***

   You failed to conduct the clinical investigation of [redacted] in accordance with the investigational plan and protocol. For example, you failed to follow the protocol for the randomization of patients. The protocol states that patient numbers will be assigned consecutively by chronological order of entry into the study. According to the patient enrollment log, patients 1 through 17 were not enrolled into the study in chronological order. The patient numbers and surgery dates for the first seventeen patients entered into the study are listed in the enrollment log as follows:

Patient	Surgery Date	Patient	Surgery Date
1	05-07-96	10	06-24-96
2	05-08-96	11	07-02-96
3	05-20-96	12	07-05-96
4	05-17-96	13	07-08-96
5	05-16-96	14	09-03-96
6	05-15-96	15	08-01-96
7	05-21-96	16	08-02-96
8	05-28-96	17	08-22-96
9	06-03-96		

In addition, you deviated from the protocol by failing to properly report all patient concomitant medications on study case report forms. For example, patient [redacted] reported on the two-month post-operative weekly patient diary injections of [redacted] on [redacted]. This information was not reported on the Interval History case report form for the assessment date of [redacted]

3. **Failure to submit to the IRBs for review and approval changes in the investigational plan** ***(21 CFR 812.35).***

You failed to submit to the IRBs changes in the investigational plan. For example, the original study protocol was approved by the [redacted] IRB on January 30, 1996, and approved by the [redacted] IRB on June 5, 1996. Subsequent protocol versions dated November 1996, and March 1998 were not submitted to either IRB for review and approval.

The violations listed above are not intended to be an all-inclusive list of deficiencies at your site. As a clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations. To assist you, we have enclosed a copy of the *FDA Information Sheets*, guidance for clinical investigators.

Please advise this office, in writing, **within fifteen (15) working days of receipt of this letter**, of the specific steps that you have taken to correct these violations and other violations known to you, and to prevent the recurrence of similar violations in current or future studies. Failure to respond may result in regulatory action, including disqualification, without further notice.

You should direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kathleen E. Swisher, R.N., J.D., Consumer Safety Officer.

A copy of this letter has been sent to our Atlanta District Office, 60 Eighth Street, NE, Atlanta, Georgia 30309. We request that a copy of your response be sent to that office as well.

Sincerely yours,

Larry Spears
Acting Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosure

cc:

[redacted] M.D.
IRB Chairman
[redacted]
Institutional Review Board
[redacted]

[redacted] M.D.
IRB Chairman
[redacted]
Institutional Review Board
[redacted]

[redacted]
President
[redacted]